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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/849,814	YOKOZEKI ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5,7,10 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,8,9,11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/21/04 &11/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The examiner acknowledges the Response to the Restriction Requirement and Amendments to the Claims, filled Jan. 03, 2006. Claim 4 has been cancelled; claims 1, 2, 5-8 and 10-13 have been amended. Claims 1-3 in part related to the enzyme of SEQ ID NO: 12, claim 6, 8, and claim 9 in part related to Sphingobacterium, claim 11, 13, and claim 14 in part related to the enzyme of SEQ ID NO: 12 and L-alanine ester as a carboxy component are under examination. Claims 1-3 in part related to the enzyme of SEQ ID NO:6, claim 5, 7, and claim 9 in part related to Empedobacter, claim 10, 12, and claim 14 in part related to the enzyme of SEQ ID NO: 6 and carboxycomponent of a glycine ester, L-threonine ester and L-tyrosine ester and D-alanine ester are withdrawn form examiner's consideration as drawn to a nonelected invention see 37 CFR 1.142(b).

DETAILED ACTION

1. Election/Restriction

Applicant's election, with traverse, of the invention comprising claims 1-14 as directed to SEQ ID NO: 12 (Group H in the restriction requirement), and an L-alanine ester as the carboxy component of the substrate peptide (Group K in the restriction requirement) is acknowledged. However, because claim 4 has been cancelled the election refers to claims 1-3 and 5-14.

Because of the amendments to the claims and persuasive arguments restriction between Groups A-C are withdrawn. Restriction between Group D-F is moot because claim 4 is canceled. Restriction between Groups I and J was issued in error, because

the sequence listing comprises one enzyme from Empedobacter which is SEQ ID NO:6, and one enzyme of Sphingobacterium which is SEQ ID NO:12.

In summary, claims 1-3 in part related to the enzyme of SEQ ID NO: 12, claim 6, 8, and claim 9 in part related to Sphingobacterium, claim 11, and claim 13 and 14 in part related to the enzyme of SEQ ID NO: 12 and L-alanine ester as carboxy component are under examination. Claims 1-3 in part related to the enzyme of SEQ ID NO:6, claim 5, 7, claim 9 in part related to Empedobacter, claim 10, 12, and claim 3 related to any amino acid ester which is not L-alanine ester and to amino acid amide, and claim 14 in part related to the enzyme of SEQ ID NO: 6 and a glycine ester, L-threonine ester and D-alanine ester are withdrawn form examiner's consideration as drawn to a nonelected invention; see 37 CFR 1.142(b).

The methods of using the enzyme of SEQ ID NO: 12 and 6 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are two methods of using two different products. The methods are not disclosed as capable of use together. For these reasons restriction between the methods of use of SEQ ID NO: 6 and 12 is proper and made FINAL.

2. Priority

Acknowledgment is made of applicants' claim for priority based on application JP 2002-218958, filed 07/26/2002. Priority document has been filed, however, because

the applicants have not provided translations it is uncertain whether the elected subject matter is disclosed. It is also unknown who is the author on the priority documents, and who is the assignee. Thus, the priority has not been granted.

3. Objections

3.1. Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

3.2. Claims

Claim 11 and 13 are objected to for using the term "base sequence" to mean "nucleotide sequence". Please correct both claims.

Claims 6, 8, 11 and 13 are objected to for the protein names (C), (D), (G), (H), and DNA names (c), (b), (g) and (h), which are unnecessary and confusing.

The language of claim 2 in line 3 should be corrected, because it is not clear whether the microbe or the enzyme uses as substrates an amine component and a carboxy component.

4. Rejections

4.1. 35 USC, section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 6, 8, 11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 and 13 are rejected because whithout listing the conditions explicitly, they are unclear in recitation " hybridizes....under stringent conditions". There are many sets of stringent hybridzation conditions in the art that are used for selecting DNA molecule by hybridization. It is noted that description of an example of hybridization conditions is given in the specification on page 27. However, conditions are merely exemplified and there is nothing to suggest that other hybridization conditions are not intended to be included. In the art what conditions are considered "stringent" varies widely depending on the experiment and person making the determination. Therefore, it is unclear how homologous to a sequence encoding SEQ ID NO: 11 a sequence must be to be within the scope of the claim. Specifying the hybridization conditions in the claims will overcome this rejection.

In addition, claims 6 and 8 are rejected as unclear. The disclosure fails to define what is the meaning of the term "inversion of one or a plurality of amino acids". The term inversion is not standard in the art with regard to types of mutations and this is unclear as to what types of changes are encompassed.

4.3. 35 USC, section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4.3.1. Lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-3, 6, 8, 9, 11 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3 and dependent claims 9 and 14 are rejected as directed to a genus of methods using a genus of enzymes forming peptides comprising three or more amino acid residues. The genus is lacking sufficient written description of structure. The broadly claimed methods recite use of any peptide forming enzyme form any organism or man-made, whereas the disclosure provides only two species, i.e., the enzyme from Sphingobacterium identified by SEQ ID NO: 12 and SEQ ID NO:6. Providing amino acid sequence set forth as SEQ ID NOs: 12 and 6 is not sufficient to identify the structure of the large genus of enzymes as a whole. One having skills in the art is not convinced that the Applicants were in possession of the claimed invention at the time the Application was filed.

Claims 6, 8, 11 and 13 are included in this rejection because they do not correct the language of the claims from which they depend.

Claims 1-3, 6, 8, 9, 11-14 are rejected as directed to a genus of methods of producing peptides from any carboxy component or L-alanine ester and any amine component. On page 13, line 15 to page 14 line 18 of the specification Applicants describe the substrates of the enzymes. However, the description uses exemplary language and for that matter it is not certain which carboxy and amine components are included and which are excluded from the genera of carboxy and amine components that actually may be substrates for the enzyme used in the clamed method. One of skills in the art realizes it is highly unlikely that the peptide forming enzyme is not specific as to the particular donors to be used as carboxy and amino components. Substrate specificity is the basic feature of enzymes. Applicants, in Tables 17-1 to 17-4

and Table 18, list 14 species of carboxy components and 24 species of amino components as substrates of the enzyme from Sphingobacterium of SEQ ID NO:12. These species do not identify the large genera of chemical compounds exemplified on page 13 and 14 of the specification. In conclusion, one of skills in the art is not convinced that any L- and D- amino acid ester and amide as exemplified on page 13 can be used by the method. In conclusion, a skilled artisan is not convinced that Applicants were not in possession of the broadly claimed invention at the time the application was filed.

In addition, claims 6 and 8 are rejected, because they are directed to a method of use of an enzyme which is a protein or a mature protein having

1) an amino acid sequence including substitution, deletion, insertion, addition, and/or inversion of one or a plurality of amino acids in amino acid residues numbers 21-619 of SEQ ID NO: 12 , or

2) an amino acid sequence including substitution, deletion, insertion, addition, and/or inversion of one or a plurality of amino acids in the amino acid sequence described in SEQ ID NO: 12.

The claims are directed to a large and variable genera of proteins the structure of which is not sufficiently disclosed in the specification and claims. The specification discloses only a single representatives for each of two claimed genera, which are polypeptides consisting of SEQ ID NO:12 or amino acid nucleotides 21-619 of SEQ ID NO:12 (a mature form). Disclosing these two amino acid sequences is, however,

insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genera 1) and 2). No information, beyond the characterization of both genera as having peptide forming activity has been provided by Applicants. This limited characteristics, however, does not indicate that Applicants had possession of the claimed genera of these modified polypeptdes. The specification does not contain any disclosure of the structure of all variants, i.e., the polypeptide sequences derived from SEQ ID NO: 12, by substitution, deletion, insertion, addition and/or inversion of one or a plurality of amino acids of SEQ ID No: 12 of its mature form. What is more important the disclosure fails to provide the relationship between function and structure of SEQ ID NO: 12. One skilled in the art realized that a change of even one amino acid residue the sequence can render the protein inactive or can change the type of enzymatic activity.

In summary, the predictability of the structure of the species of the claimed genera is not apparent and one skilled in the art is not convinced that Applicants were in possession of the claimed invention at the time the application was filed.

4.3.2. Scope of enablement

Claims 1-3 and dependent claims 9 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of using the enzyme of SEQ ID NO:12 from the Sphingobacterium, does not reasonably provide enablement for using any enzyme having peptide forming ability. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses a method of producing a peptide having three or more amino acid residues using an enzyme having peptide forming ability, wherein the enzyme is obtained from any natural or man-made sources. Although cloning DNA encoding enzymes, expressing them, testing the expressed proteins for the ability of peptide forming is well known in the art and the skills of artisans are highly developed, to make the invention as claimed, a skilled artisan is forced to experimentation which is not routine, absent teaching the structure of the enzyme to be used. Providing only one enzyme having the necessary activity, i.e., the enzyme identified by SEQ ID NO:12, encoded by DNA of SEQ ID: 11, is not a sufficient instruction for obtaining any peptide forming enzyme, and leads to experimentation with a low probability of success. In result, without a further guidance

on the part of Applicants with regards to the structure of the enzyme used in the claimed invention experimentation left to those having skills in the art is improperly extensive and undue.

In addition, claims 1-3, 6, 8, 9, 11-14 are rejected under this paragraph because although the specification is enabling for production of the peptides using L-alanine ester as the carboxy component and 24 compounds as amino components (Tables 17 and 18), the specification is not enabling for use of any amino component and any carboxy component as claimed; see the above rejection for lack of written description. One of skills in the art realizes it is highly unlikely that the peptide forming enzyme is not specific as to the particular donors to be used as carboxy and amino components. Substrate specificity is the basic feature of enzymes and is well illustrated in Tables 17-18 presenting the efficiency of product formation from different components. The efficiency may differ more than thousand times and in some cases may be indefinitely large (for trace amounts of products). Thus, instruction given by Applicant's own data teach that not every amino component and not every carboxy component can be used to practice the claimed invention. One having skills in the art concludes that without further guidance regarding the chemical nature of the carboxy and amino component to be used in enzymatic reaction one skilled in the art is left with experimentation that is not routine, has low probability of success and undue.

Furthermore, claims 6 and 8 are rejected, because the specification, while being enabling for a method of use of an enzyme which is a protein or a mature protein set

forth by SEQ ID NO:12 or amino acid residues 21- 619 of SEQ ID NO: 12, does not reasonably provide enablement for a method of using an enzyme that has an enzyme

1) an amino acid sequence including substitution, deletion, insertion, addition, and/or inversion of one or a plurality of amino acids in amino acid residues numbers 21-619 of SEQ ID NO: 12 , or

2) an amino acid sequence including substitution, deletion, insertion, addition, and/or inversion of one or a plurality of amino acids in the amino acid sequence described in SEQ ID NO: 12.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims covers the use of any variant of the enzyme consisting of amino acid residues 21-619 of SEQ ID NO:12 or any variant of SEQ ID NO:12. Although techniques of modifications of amino acid sequences are well developed, and skills of artisans high, the lack of disclosure of function/structure of SEQ ID NO: 12 force one skilled in the art to experimentation which is not routine. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the protein variants have peptide forming ability. The provision of SEQ ID NO: 12 or amino acid residues 21-619 of SEQ ID NO:12 fails to provide such guidance of polypeptides with major structural variations therefrom which remain encompassed within the scope of the

rejected claims. Without a further guidance on the part of Applicants with regards to the structure of the variants of the enzyme to be used in the claimed method experimentation left to those skilled in the art has a low probability of success, thus it is improperly extensive and undue.

In addition, claims 11 and 13 are rejected because the specification, while being enabling for a method of use of an enzyme encoded be the DNA molecule of SEQ ID NO:11 encoding the enzyme of SEQ ID NO:12, does not reasonably provide enablement for a DNA molecule that hybridizes under stringent conditions with a DNA molecule complementary to nucleotides 61-1917 or 121-1917 of SEQ ID NO:11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The nature and breath of invention encompass a large number of DNA molecules selected under stringent conditions. In the art, there is a large number of sets of stringent hybridization conditions. The choice of a particular set depends on the experiment and the experimenter's preferences. In result, although the hybridization assays are well developed and skill of artisans high, without explicitly stated what conditions are to be used for the isolation of the claimed DNA, experimentation left to one skilled in the art has a low probability of success. Applicants teach, on page 27 specific hybridization conditions. However, this is only an example and there is nothing to suggest the other conditions are included or excluded from the claims. In summary, whithout explicitly stating what hybridization condition assure that the encoded protein

has the required activity of peptide forming the experimentation left to the skilled artisan is extensive, improper and undue.

5. Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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